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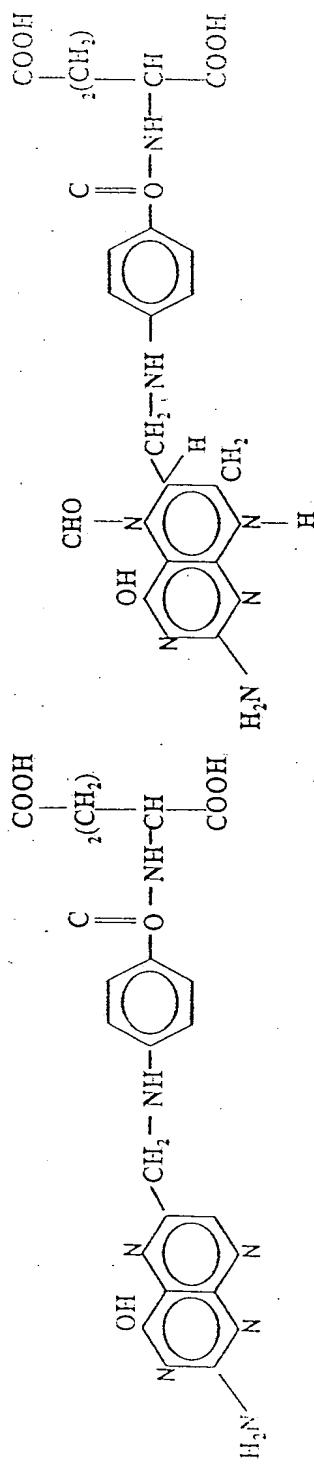
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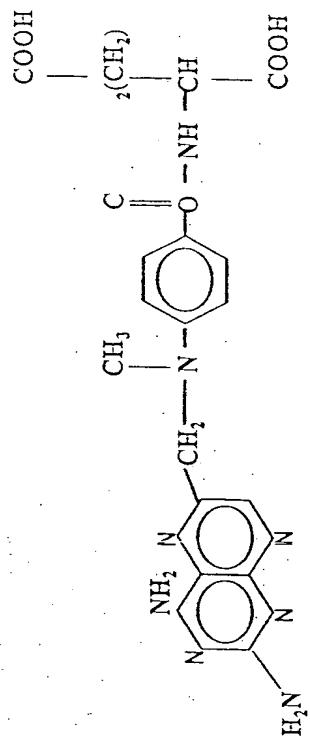
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Folates and Methotrexate



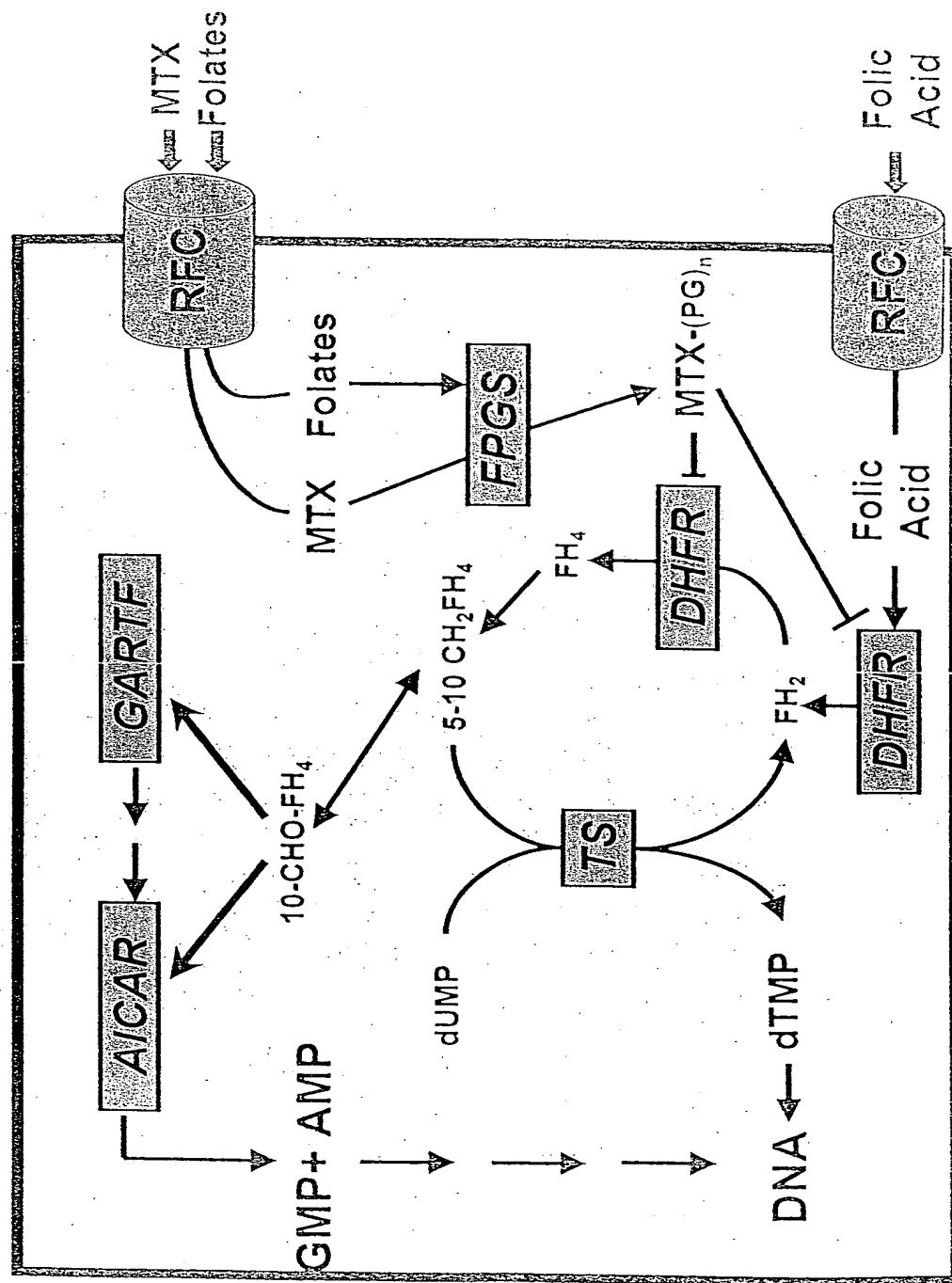
Folic Acid

5-formyl tetrahydrofolate (leucovorin)



Methotrexate (MTX)

Fig. 2



F5-3

Protocol for Genomic PCR-SSCP Analysis of Human RFC

Tumor Specimens; Tumor cell lines; Blood



Isolate Genomic DNA



Genomic PCR



SSCP Analysis & Detection of Electrophoretic Mobility Change



T/A Cloning and Sequencing



Direct DNA Sequencing



Identify the Genetic Alteration(s)



Point mutation(s) and/or Polymorphism



In-Vitro Mutagenesis



Transfect the Mutated RFC cDNA into Transport Null Cells



Measure MTX/folate Transport

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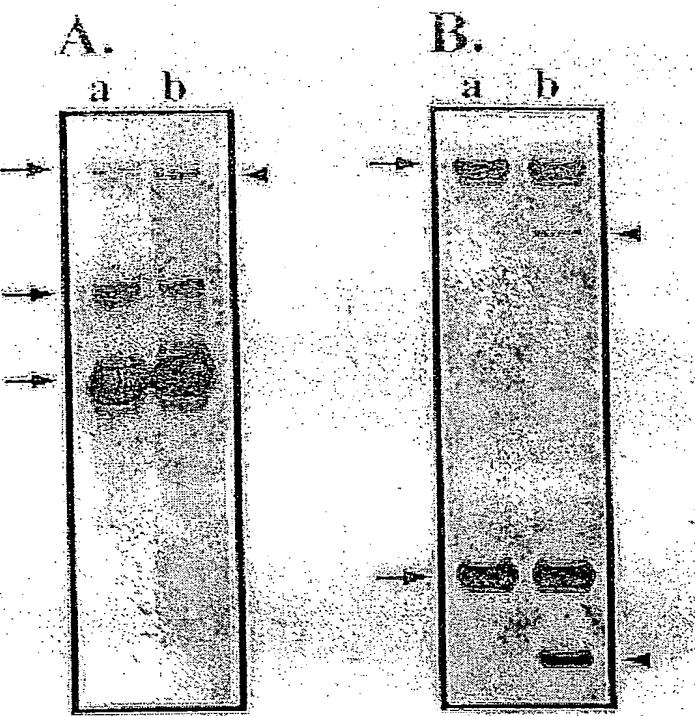


Fig. 4a

Fig. 4b

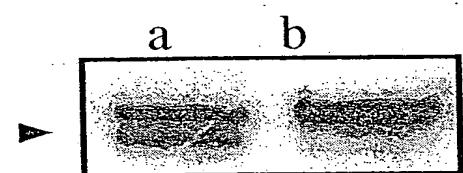
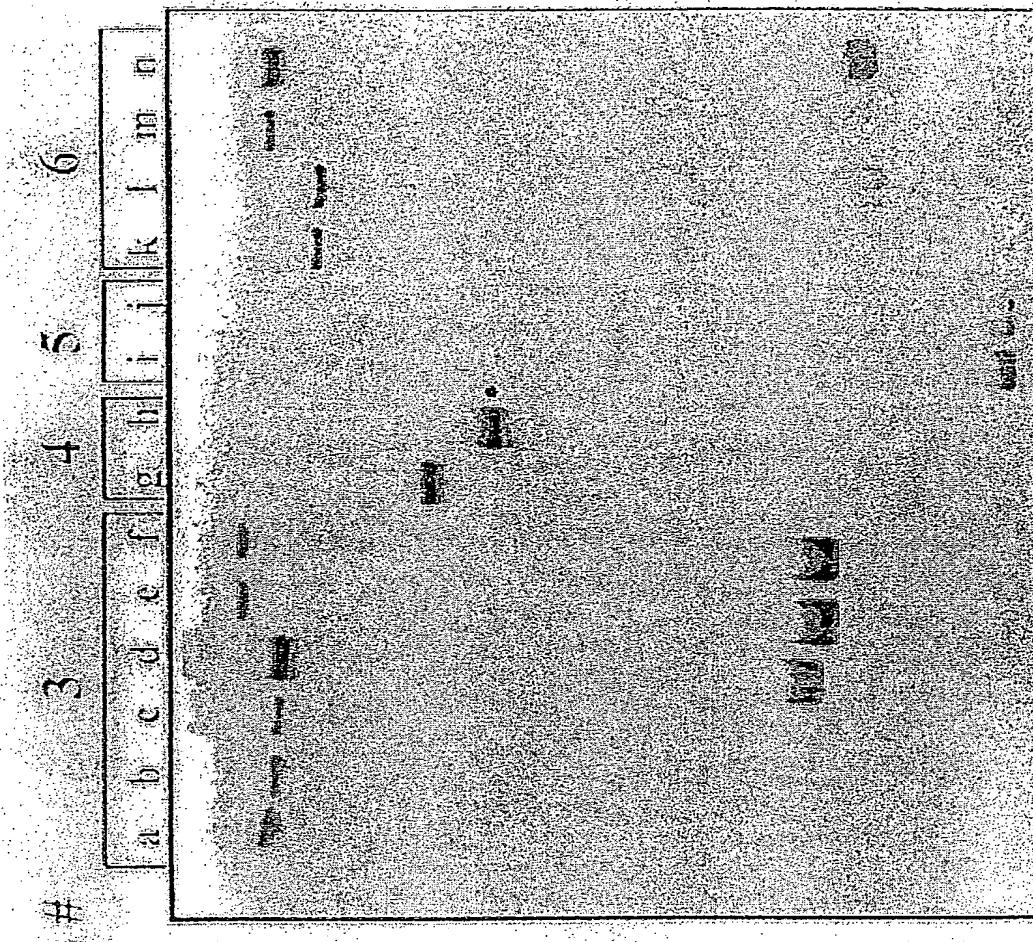


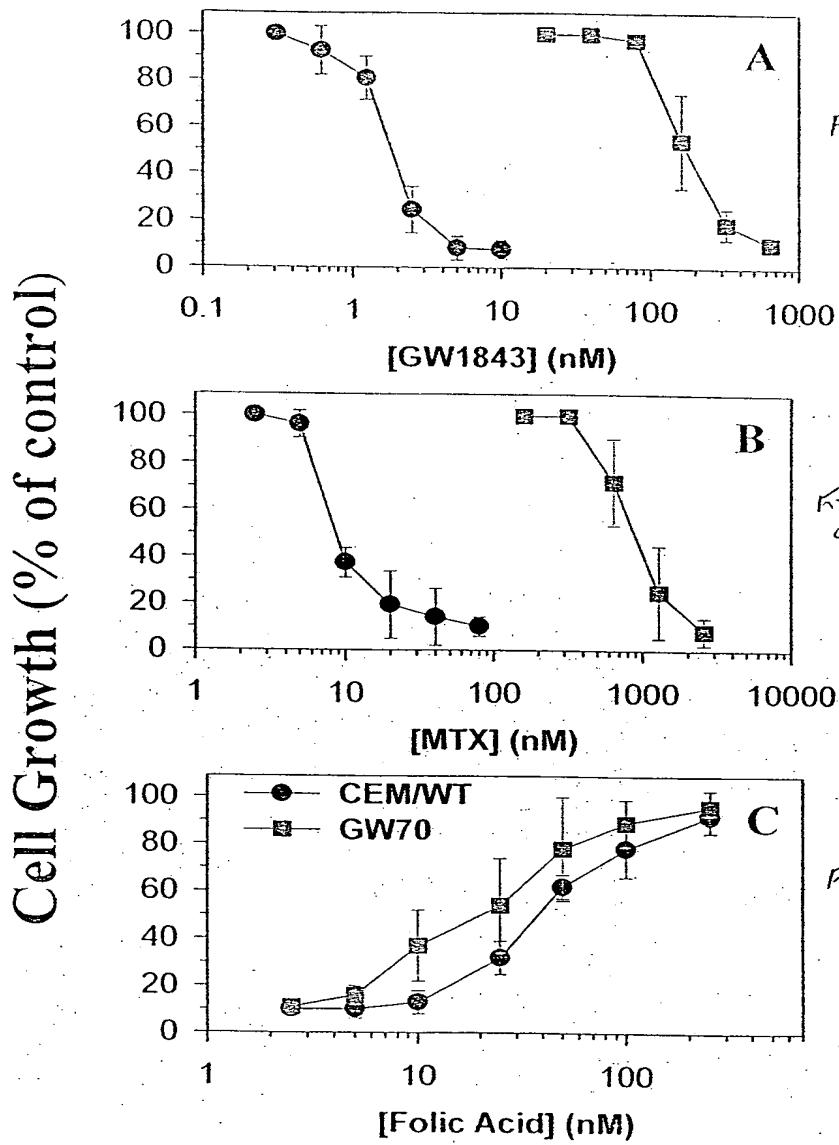
Fig. 4c

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Exon #

F63



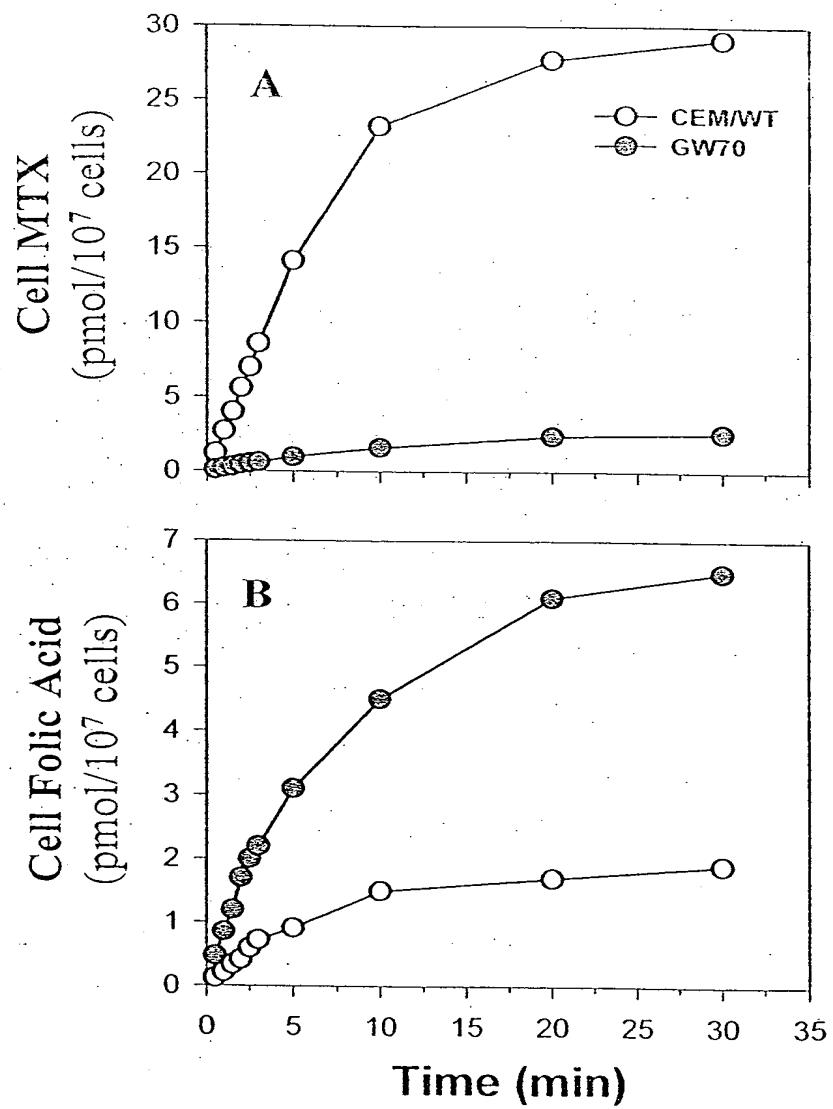
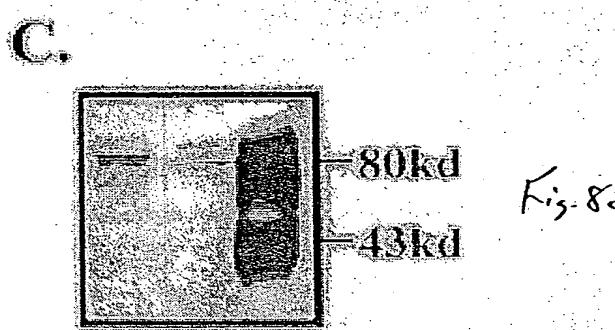
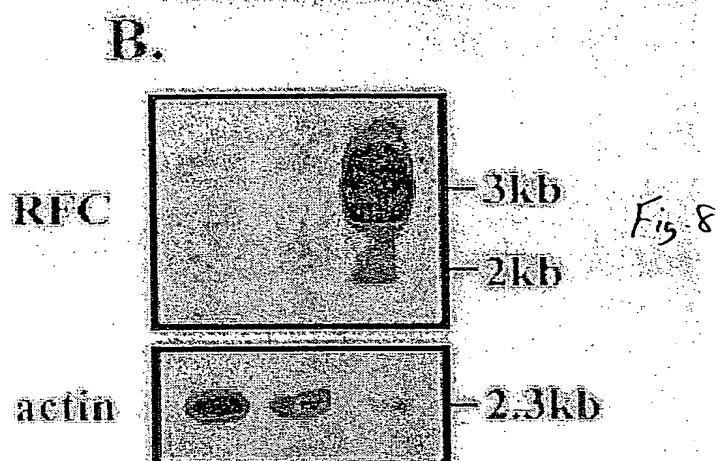
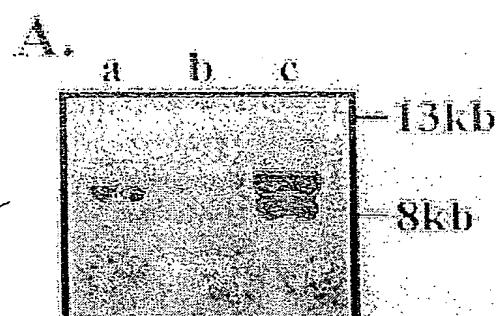


Fig. 7a

Fig. 7b

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A. Exon 2

a b c

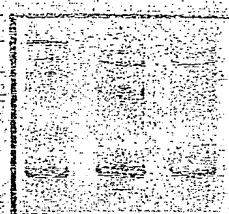


Fig 9a

B. Exon 3

a b c

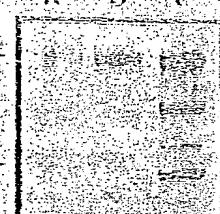


Fig 9b

C.

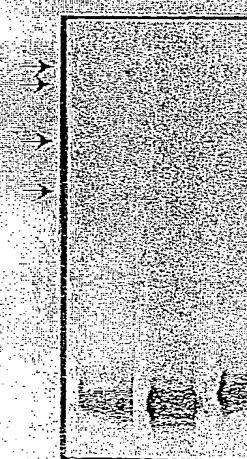


Fig 9c

D.

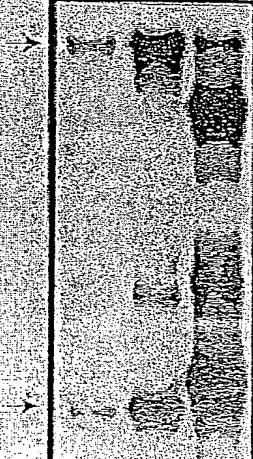


Fig 9d

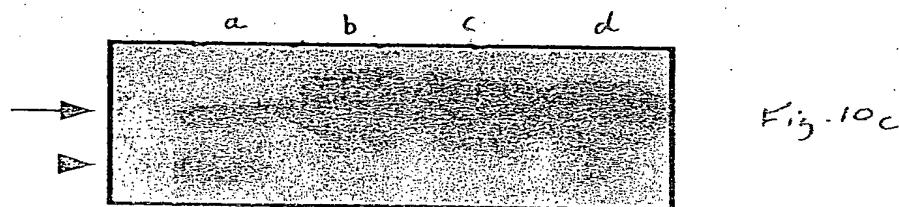
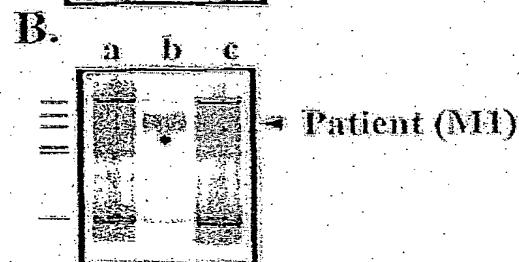
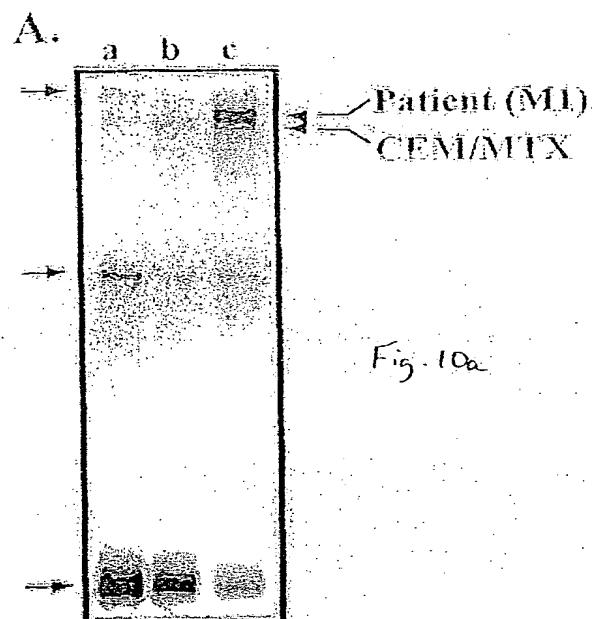


Fig. 10d

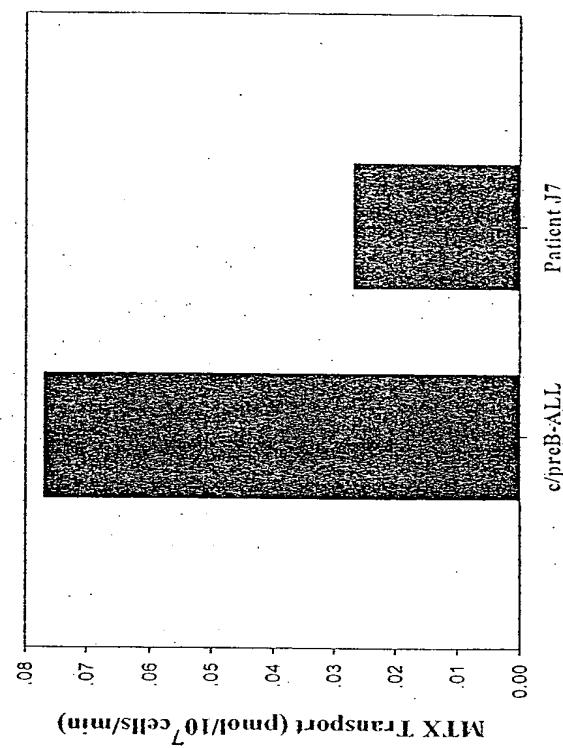


Fig. 11a

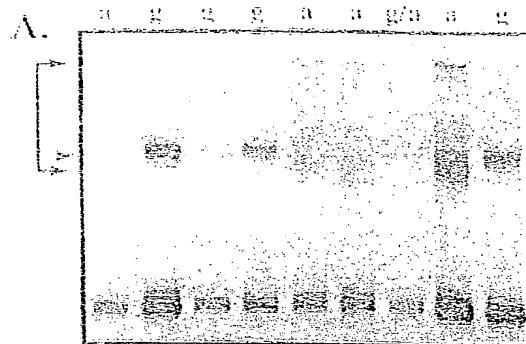
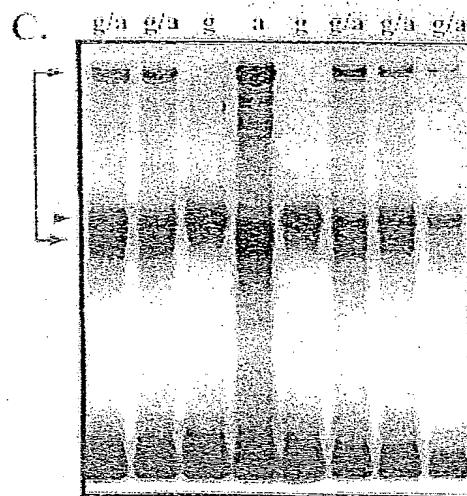
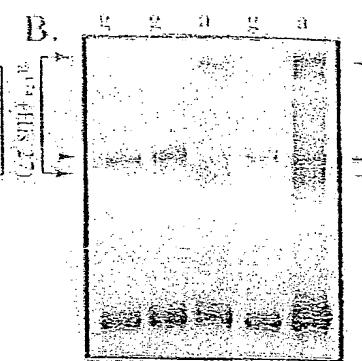
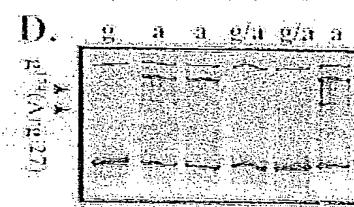


Fig. 11b



g¹²⁹(Arg 27)
R₁₂₉(Arg 27)



R₁₂₉(Arg 27)

Fig. 11c

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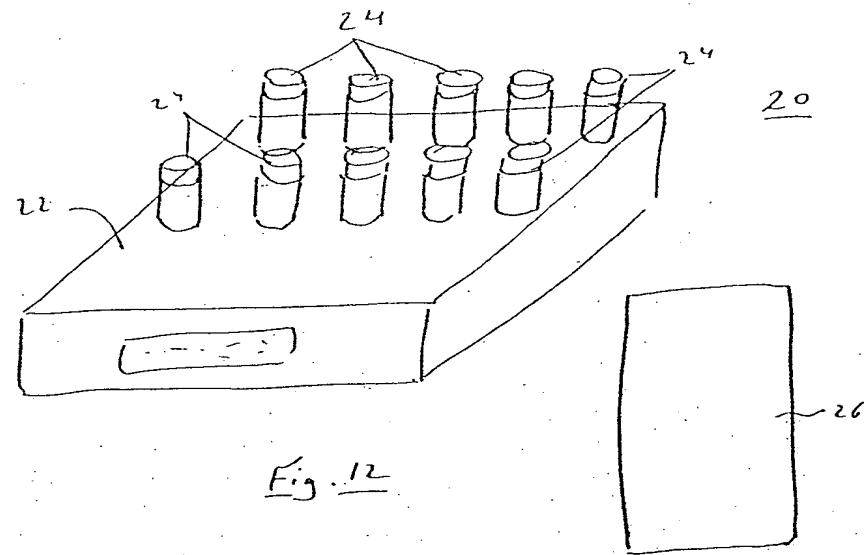


Fig. 12

09/936794

Fig. 3

